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EXAMINER	
EPPERSON, JON D	

ART UNIT	PAPER NUMBER
1639	

DATE MAILED: 11/17/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/057,828	LI ET AL.	
	Examiner	Art Unit	
	Jon D Epperson	1639	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *28 July 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-22* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-22* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Status of the Application

1. The Response filed July 28, 2004 is acknowledged.

2. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Status of the Claims

3. Claims 1-80 were pending. Applicants amended claim 1 and canceled claims 23-80. Therefore, claims 1-22 are pending and examined on the merits.

Withdrawn Objections/Rejections

4. All objections with regard to the specification are withdrawn in view of Applicants' arguments and/or amendments. The rejections under 35 U.S.C. 112, second paragraph are withdrawn in view of Applicants' arguments and/or amendments. The Kauffman et al. rejections (i.e., based on U.S. Patent No. 6,100,035) under 35 U.S.C. § 102(b) and 35 U.S.C. § 103(a) are withdrawn in view of Applicants' amendments and/or arguments. All other rejections are maintained and the arguments are addressed below.

Outstanding Objections and/or Rejections

Claim Rejections - 35 USC § 112

5. Claims 1-22 are rejected under 35 USC 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Applicant is directed to the Guidelines for the Examination of Patent Applications Under the 35 USC 112, ¶ 1 "Written Description" Requirement, Federal Register, Vol. 66, No. 4 pages 1099-1111, Friday January 5, 2001. This is a written description rejection.

Applicants' newly amended claims are directed to a broad genus of nucleic acids that comprise a promoter, cis element (which binds to transcription factor) and reporter. Such claims represent enormous scope because no structural limitations are provided for the promoter, reporter, cis element and/or any other portion of said nucleic acid. Thus, virtually an infinite number of sequences are currently claimed.

In contrast, Applicants do not provide a single working example of the claimed invention (i.e., not one full-length sequence is provided, nor is any library shown). Applicants list a few known cis elements/reporters that might be useful in making the claimed invention (e.g., see Figure 2, cis elements/reporter sequences listed as PP01 through PP30; see also page 18, lines 15-21 wherein Applicants' disclose a "laundry list" of promoters), but do not provide any full-length sequences incorporating said cis elements/reporters nor do they provide any data that such sequences were ever made and/or used to make the claimed library.

With regard to the description requirement, Applicants' attention is directed to The Court of Appeals for the Federal Circuit (CAFC) which held that a "written description on an invention

involving a chemical genus, like a description of a chemical species, 'requires a precise definition, such as by structure, formula [or] chemical name,' of the claimed subject matter sufficient to distinguish it from other materials." *University of California v. Eli Lilly and Co.*, 43 USPQ2d 1398, 1405 (1997), quoting *Fiers v. Revel*, 25 USPQ2d 1601, 1606 (Fed. Cir. 1993) (bracketed material in original)[The claims at issue in *University of California v. Eli Lilly* defined the invention by function of the claimed DNA (encoding insulin)] (the case is referred to herein as "*Lilly*"). In addition, when there is substantial variation within the genus, one must describe a sufficient variety of species to reflect the variation within the genus (e.g., see MPEP § 2163.05).

In the present case, Applicants claim virtually an infinite number of nucleic acid sequences from every known species containing promoters/reporters/cis-elements that are only functionally defined (i.e., their ability to act as a promoter, reporter or cis-element). Thus, Applicants' claims are broader in scope than those that were held to be impermissible in *Lilly* because, unlike *Lilly*, Applicants' claims encompass virtually an infinite number of sequences. In addition, Applicants provide even less guidance than was held to be impermissible in *Lilly* because Applicants do not even provide a single working example of the claimed invention. In addition, Applicants have not provided any guidance on how the various elements of the claimed nucleic acid sequences interact, which adds enormous uncertainty and variability (e.g., which promoter must be used with a given cis-element and how far apart should these two elements be placed). Consequently, one of skill in the art would not reasonably conclude that Applicants' were in possession of the claimed genus because the genus is enormous and highly variant and Applicants have not provided even a single working example that falls within this claimed scope.

Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method of isolating it and/or making it. The compound itself is required. See *Fiers v. Revel,* 25 USPQ2d 1601 at 1606 (CAFC 1993) and *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd., 18* USPQ2d 1016.

The Federal Circuit has also stated that a written description of an invention requires a precise definition, one that defines the structural features of the chemical genus that distinguishes it form other chemical structures. A definition by function does not suffice to define the genus because it is only an indication of what the chemical does, rather than what it is. The language of the specification should describe the claimed invention to that one skilled in the art can recognize what is claimed. A description of a compound in terms of its function fails to distinguish the compound from others having the same activity or function. A description of what a material does, rather than of what it is, usually does not suffice. The disclosure must all one skilled in the art to visualize or recognize the identity of the subject matter purportedly described. *University of California v. Eli Lilly and Co.* (U.S. Court of Appeals Federal Circuit (CAFC) 43 USPQ2d 1398 7/22/1997 Decided July 22, 1997; No. 96-1175).

Here, Applicants have not provided *sufficient* structural features (e.g., a cis-acting "consensus" sequence and/or "core" structure) that would allow a person of skill in the art to distinguish it from other sequences. Furthermore, the Examiner contends that no such structure/function correlation exists for the claimed scope because the art is highly unpredictable. Thus, a person of skill in the art could not "immediately envision" and/or "obtain" the claimed sequences because no "structure/correlation function" exists and "no conditions" for the obtainment of said sequences have been provided. In is noted that in *Fiers v. Sugano* (25

USPQ2d, 1601), the Federal Circuit concluded that "... if inventor is unable to envision detailed chemical structure of DNA sequence coding for specific protein, as well as method of obtaining it, then conception is not achieved until reduction to practice has occurred, that is until after gene has been isolated ... conception of any chemical substance, requires definition of that substance other than by its functional utility." Therefore, Applicants were not is possession of the claimed genus.

Response

6. Applicant's arguments directed to the above written description rejection were fully considered (and are incorporated in their entirety herein by reference) but were not deemed persuasive for the following reasons. Please note that the above rejection has been modified from it original version to more clearly address applicants' newly amended and/or added claims and/or arguments.

[1] Applicants argue, "Eli Lilly is inapplicable ... [because] it is directed to a nucleotide sequence encoding a protein ... [whereas] Applicants claim a library of nucleic acid constructs" (e.g., see 7/28/04 Response, page 5, section II).

[2] Applicants argue, "The specification provides ample examples of what the library is and how to construct the library" and specifically refer the Examiner's attention to pages 13-16, figures 1A, 1B and 2 and pages 16-20 (e.g., see 7/28/04 Response, pages 5-6).

This is not found persuasive for the following reasons:

[1] The Examiner contends that Applicants' interpretation of *Lilly* is too narrow and is not supported by the MPEP and/or relevant case law. For example, MPEP § 2163.05 states that when there is substantial variation within the genus, one must describe a sufficient variety of

species to reflect the variation within the genus (regardless of whether the genus is drawn to a nucleic acid that encodes a protein or not), which has not been done (e.g., see rejection above).

In addition, the combined holdings of *Enzo*, *Lilly*, and *Fiers* are not limited to claims directed to DNA or nucleic acid sequences that encode for proteins as Applicants contend. This assertion is simply not supported by case law. In *Fiers*, for example, the Court of Appeals stated that "conception of a DNA, like conception of ***any chemical substance***, requires a definition of that substance other than by its functional utility," 984 F.2d at 1169. Although the court there was discussing conception rather than written description, the court also stated that "[i]f a *conception* of a DNA requires a precise definition, such as by structure, formula, chemical name, or physical properties, as we have held, then a *description* also requires that degree of specificity," since "one cannot describe what one has not conceived." *Id.* at 1171 (emphasis added).

In *Lilly*, the court did draw a distinction between genetic material and other chemicals stating:

> a generic statement such as "vertebrate insulin cDNA" or "mammalian insulin cDNA," without more, is not an adequate written description of the genus because it does not distinguish the claimed genus from others, except by function. It does not specifically define any of the genes that fall within its definition. It does not define any structural features commonly possessed by members of the genus that distinguish them from others. One skilled in the art therefore cannot, as one can do with a fully described genus, visualize or recognize the identity of the members of the genus.

119 F.3d at 1568.

In drawing this distinction, however, the court also stated that "[i]n claims involving [non-genetic] chemical materials, generic formulae ***usually indicate with specificity what the generic claims encompass***. One skilled in the art can distinguish such a formula from others and *can identify many of the species* that the claims encompass. Accordingly, such a formula is

normally an adequate description of the claimed genus." *Id.* (emphasis added). In the present case, Applicants provide no such specificity, nor could one skilled in the art identify any particular compound encompassed by the claims because the art is highly unpredictable. To the contrary, the specification states that suitable compounds *might* be found from among a list of potential cis-elements and reporter sequences, but do not provide any actual working examples.

The *Lilly* court also stated that "[t]he description requirement of the patent statute requires a description of an invention, not an indication of a result that one might achieve if one made that invention." *Id.* This statement was ***not qualified by reference to genetic material***, and the case cited by the court in support of that statement, *In re Wilde*r, 736 F.2d 1516 (Fed. Cir. 1984), *cert. denie*d, 469 U.S. 1209 (1985), did not involve any chemical-related claims, but claims directed to a mechanism for indicating the location of information recorded on a dictating machine. The *Wilder* court affirmed the PTO's rejection of those claims because the specification did "little more than outlin[e] goals appellants hope the claimed invention achieves and the problems the invention will hopefully ameliorate." *Id.* at 1521.

The *Enzo* court likewise did not indicate that its holding was limited to claims involving DNA that encode a protein. It is noteworthy that neither of the examples given by the court of insufficient descriptions were descriptions of genetic material (e.g., examples of "an anti-inflammatory steroid" and "an antibiotic penicillin" were provided).

Furthermore, to the extent that the *Enzo* court held that a functional description can meet the written-description requirement, it did so in accordance with PTO guidelines stating that the requirement can be met by disclosing "sufficiently detailed, relevant identifying characteristics," including "functional characteristics when *coupled* with a known or disclosed correlation

between function and structure ... ." No such correlation has been disclosed here (emphasis added).

Consistent with that standard, the central holding of *Enzo* was that with respect to "biological materials," *id.* at 1325, (a term which presumably encompasses more than simply genetic material), "reference in the specification to a deposit in a public depository, which makes its contents accessible to the public when it is not otherwise available in written form, constitutes an adequate description of the deposited material sufficient to comply with the written description requirement of § 112, ¶ 1." *Id.* In other words, it is not be necessary to give a precise chemical formula or description of a chemical structure when persons of ordinary skill in the art can ascertain what substance is being described by resort to the public depository where a specimen of that substance is kept. In the case at bar, however, no such deposit has been made.

[2] The Examiner contends that Applicants have not provided a single working example of the claimed invention. None of the cited passages (e.g., page 13-16, figures 1A, 1B and 2, pages 16-20) show a library of nucleic acid constructs that comprising a promoter, reporter, cis-element, etc as outlined by the current claims. Applicants cited passages merely provide a laundry list of "separate" known nucleic acid cis elements, reporters and/or promoters that "might" work with the claimed invention. A lack of adequate written description issue also arises if the knowledge and level of skill in the art would not permit one skilled in the art to immediately envisage the product claimed from the disclosed process. See, e.g., Fujikawa v. Wattanasin, 93 F.3d 1559,1571, 39 USPQ2d 1895, 1905 (Fed. Cir. 1996) (a "laundry list" disclosure of every possible moiety does not constitute a written description of every species in a genus because it would not "reasonably lead" those skilled in the art to any particular species).

In re Ruschig, 379 F.2d 990, 995, 154 USPQ 118, 123 (CCPA 1967) ("If n-propylamine had been used in making the compound instead of n-butylamine, the compound of claim 13 would have resulted. Appellants submit to us, as they did to the board, an imaginary specific example patterned on specific example 6 by which the above butyl compound is made so that we can see what a simple change would have resulted in a specific supporting disclosure being present in the present specification. The trouble is that there is no such disclosure, easy though it is to imagine it.") (emphasis in original); Purdue Pharma L.P. v. Faulding Inc., 230 F.3d 1320, 1328, 56 USPQ2d1481, 1487 (Fed. Cir. 2000) ("the specification does not clearly disclose to the skilled artisan that the inventors ... considered the ratio... to be part of their invention .... There is therefore no force to Purdue's argument that the written description requirement was satisfied because the disclosure revealed a broad invention from which the [later-filed] claims carved out a patentable portion").

Accordingly, the written description rejection cited above is hereby maintained.

New Rejections

Claims Rejections - 35 U.S.C. 112, first paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

7. Claim 1 is rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled

in the relevant art that the inventor(s), at the time the application was filed had possession of the claimed invention. This is a new matter rejection.

A. Claim 1 was amended in the 7/28/04 Response to recite, " a cis element to which a transcription factor is known to bind" (e.g., see newly amended claim 1). However, applicant did not show where support for this amendment can be found in the specification. The Examiner contends that there is no support for this amendment. If applicant believes this rejection is in error, applicant must disclose where in the specification support for this amendment can be found in accordance with MPEP 714.02.

B. Claim 1 was amended in the 7/28/04 Response to recite, "a reporter sequence that is 3' relative to the promoter sequence and comprises a variable sequence that varies within the library o nucleic acid constructs" (e.g., see newly amended claim 1). To the extent that the phrase "a reporter sequence that is 3' relative to the promoter sequence and comprises a variable sequence" no longer further limits the reporter sequence (i.e., the previous limitation required that the reporter sequence comprise the variable sequence), but now more broadly limits the nucleic acid construct (i.e., an portion of the nucleic acid may now contain the variable region), the increased breadth of possible modification constitutes new matter, since there is no specification support or original claim support for such scope; nor has applicant provided any indication where such support exists. If applicant believes this rejection is in error, applicant must disclose where in the specification support for this amendment can be found in accordance with MPEP 714.02.

Claims Rejections - 35 U.S.C. 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless -
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

8. Claims 1-13 and 20 are rejected under 35 U.S.C. 102(b) as being anticipated by Kauffman et al. (WO 00/04196) (Date of Patent is **January 27, 2000**) (see 3/11/04 IDS).

For ***claim 1***, Kauffman et al. (see entire document) disclose "cis acting nucleic acid elements and methods of use" (e.g., see Kauffman et al., title and abstract), which anticipates claim 1. For example, Kauffman et al. disclose a library of nucleic acid constructs, each construct comprising a cis element sequence comprising one or more copies of a cis element to which a transcription factor is known to bind (e.g., see claim 38, A plurality of isolated nucleic acid molecule [i.e., a library], each isolated nucleic acid molecule comprising one or more cis acting nucleic acid elements"; see also page 1, lines 29-30, "As an example, regulatory proteins called 'transcription factors' bind to cis acting nucleic acid elements"; see also page 2, line 5; see also page 14, last paragraph; see also page 9, paragraph 2; see also pages 5-6). Kauffman et al. also disclose variation within the cis element sequence (e.g., see page 13, paragraph 1, "As an example, a population that includes all possible molecules of between 5 and 20 nucleotides in length, including each of the four naturally occurring nucleotides at each position, would have

approximately … 10^{13} different nucleic acid molecules. Such a population … inherently includes all possible cis acting nucleic acid elements of up to about 20 nucleotides in length"; see also page 8, first full paragraph; see also page 11, last paragraph; see also page 50, first full paragraph). Kauffman et al. also disclose a promoter sequence 3' relative to the cis element sequence (e.g., see page 9, last paragraph, "A cis acting nucleic acid element can be localized within the nucleic acid sequence it regulates, or upstream or downstream thereof"; see also page 3, paragraph 1). Kauffman et al. also disclose a reporter sequence that is 3' relative to the promoter sequence (e.g., page 14, first full paragraph, "If desired, some or all of the isolated nucleic acid molecules can … be flanked at one or both ends by … detectable sequences [i.e., reporter molecules]"; see also paragraph bridging pages 50-51, "… a plurality of isolated nucleic acid molecules containing cis acting nucleic acid elements can be … enhancers and promoters … or any other set of nucleic acid cis acting elements"). In addition, Kauffmann et al. disclose a variable sequence (e.g., see paragraph bridging pages 13-14; see also page 23, line 20; see also page 63, line 24; see also page 65, line 5). Finally, Kauffman et al. also disclose cis element sequences that correspond to a given reporter sequence within the library of nucleic acid constructs (e.g., see page 14, first full paragraph; see also paragraph 19, lines 13-14; see also page 34, middle paragraph; see also page 35, paragraphs 1-3; see also page 60 paragraph 1 which disclose numerous methods of detection using reporter sequences that "correspond" to the cis element i.e., allow identification of the cis element).

For ***claim 2-3***, Kauffman et al. disclose the use of conserved priming sequences (e.g., see page 14, first full paragraph, "If desired, some or all of the isolated nucleic acid molecules can include, or be flanked at one or both ends by, known sequences, such as sequences homologous to oligonucleotide primers for the polymerase chain reaction (PCR); see also page 25, last paragraph; see also page 33, first paragraph").

For ***claims 4-7***, Kauffman et al. disclose 10^{13} different cis elements (e.g., see page 13, line 25).

For ***claims 8-10***, Kauffman et al. disclose at least two copies of the cis element (e.g., see claim 38, "A plurality of isolated nucleic acid molecules, each isolated nucleic acid molecule comprising one or more [i.e., two, three, four, etc.] cis acting nucleic acid elements"; see also page 57, lines 24-25).

For ***claims 11-13***, Kauffman et al. disclose cis elements with a length between 5 and 50 base pairs (e.g., see page 10, first full paragraph, "A cis acting nucleic acid element is generally from about 4 to about 100 nucleotides in length, and is more typically from about 6 to about 25 nucleotides in length").

For ***claim 20***, Kauffman et al. disclose different reporter sequences that encode different reporter proteins (e.g., see page 3, paragraph 1; see also page 47, paragraph 1; see also column 6, paragraph 3, "see column 3, lines 46-53, "The methods are advantageous in providing a means for simultaneously identifying nucleic acid binding factors that modulate a genetic activity of a plurality of nucleic acids").

Response

To the extent that Applicants' arguments can be similarly applied to the new Kauffman et al. reference, the following comments are noted.

[1] Applicants argue, "Kauffmann et al. fails to teach the claimed library of nucleic acid construct each of which comprises one or more copies of a cis element to which a transcription factor is already known to bind" (e.g., 7/28/04 Response, page 7, last two paragraphs).

[2] Applicants argue, "Kauffman et al. also fails to teach a library of nucleic acid constructs each of which comprises a reporter sequence that is 3' relative to the promoter sequence and comprises a variable sequence that varies within the library of nucleic acid constructs" (e.g., see 7/28/04 Response, page 8, last two paragraphs).

This is not found persuasive for the following reasons:

[1] The Examiner contends that Applicants' limitation that the cis element bind to a transcription factor that is "already known" represents "intended use", which is not given any patentable weight for product claims. In addition, the Examiner contends that the current Kauffman et al. reference does teach and, if fact, claims cis elements to which known transcription factors bind (e.g., see claim 41, "A plurality of isolated nucleic acid molecules bound to nucleic acid binding factors, each isolated nucleic acid molecule comprising one or more cis acting nucleic acid elements."; see also page 14, last paragraph, "As used herein, the term 'nucleic acid binding factor' is a factor that selectively binds a cis acting nucleic acid element to modulate a genetic activity of a nucleic acid … Nucleic acid binding factors include, for example, transcription factors").

[2] The Examiner respectfully disagrees. Kauffman et al. states, "If desired, some or all of the isolated nucleic acid molecules can ... be flanked at one or both ends by ... detectable sequences [i.e., reporter molecules are at both the 3' and 5' ends of the molecule]"; see also paragraph bridging pages 50-51, "... a plurality of isolated nucleic acid molecules containing cis acting nucleic acid elements can be ... enhancers and promoters ... or any other set of nucleic acid cis acting elements" (e.g., page 14, first full paragraph). In addition, Kauffman et al. teach the use of variable sequences (e.g., see paragraph bridging pages 13-14; see also page 23, line 20; see also page 63, line 24; see also page 65, line 5).

Claim Rejections - 35 USC § 103

9. Claims 1-22 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kauffman et al. (WO 00/04196) (Date of Patent is **January 27, 2000**) (see 3/11/04 IDS) and Morris et al. (US Patent No. 6,458,530)(Filing Date is **April 4, 1996**).

For ***claims 1-13 and 20***, Kauffman et al. teach all the limitations stated in the 35 U.S.C. 102(b) rejection above (incorporated in its entirety herein by reference), which anticipates claims 1-13 and 20 and, consequently, also renders obvious claims 1-13 and 20.

The prior art teaching of Kauffman et al. differs from the claimed invention as follows:

For ***claims 14-19***, the prior art teachings of Kauffman et al. differ from the claimed invention by not specifically reciting the size of the variable sequence in the reporter e.g., at least 14 bases in length (see claim 14).

For ***claims 21-22***, the prior art teachings of Kauffman et al. do not explicitly recite an "open reading frame" although it is undoubtedly implied from the molecular cloning techniques used i.e., the reporter wouldn't be expressed without it (e.g., see column 23, line 48).

However, Morris et al. teach the following limitations that are deficient in Kauffman et al.:

For ***claims 14-19***, Morris et al. (see entire document) disclose specially selected nucleic acid tags that contain variable regions between 8 and 150 nucleotides in length for labeling molecular, cellular and viral libraries which would encompass the nucleic acid constructs of Kauffman et al. (e.g., see Morris et al., Summary of Invention; see also column 3, paragraphs 2-3; see also claim 7).

For ***claim 21***, Morris et al. disclose the use of open reading frames (e.g., see column 11, paragraph 3; see also example 1, especially column 24, lines 14-51).

For ***claim 22***, both Morris et al. and Kauffman et al. do not explicitly state that a stop codon is 3' relative to the reporters disclosed therein, but the Examiner contends that stop codons are typically used in the art and the reporter sequence would not have the proper length if it did not contain such a stopping point. "When the PTO shows a sound basis for believing that the products of the applicant and the prior art are the same, the applicant has the burden of showing that they are not." *In re Spada*, 911 F.2d 705, 709, 15 USPQ2d 1655, 1658 (Fed. Cir. 1990). The Office does not have the facilities to make such a comparison and the burden is on the applicants to establish the difference. See *In*

re Best, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977) and *Ex parte Gray,* 10 USPQ 2d 1922 1923 (PTO Bd. Pat. App. & Int.).

It would have been obvious to one skilled in the art at the time the invention was made to make and use the variable reporters as taught by Morris et al. with the cis acting nucleic acid library as taught by Kauffman et al. because Kauffman et al. explicitly states that "[n]ucleic acid chips and automated detection procedures are particularly advantageous in high-throughput screening procedures for identifying cis acting nucleic acid elements" (e.g., see Kauffman et al., column 16, lines 53-54), which would encompass the automated nucleic acid chips disclosed by Morris et al. i.e., the references represent analogous art (e.g., see Morris et al., figure 5 disclosing a nucleic acid chip). Furthermore, one of ordinary skill in the art would have been motivated to use the variable reporters as taught by Morris et al. because the variable reporters "provide a much more cost-effective approach to screening" i.e., parallel screening saves time and money (e.g., see Morris et al., column 11, lines 60-62). Furthermore, one of ordinary skill in the art would have reasonably expected to be successful because both Morris et al. and Kauffman et al. teach general methods that can use recombinant DNA optionally with PCR techniques i.e., the methods are compatible (e.g., see Kauffman et al., column 15, last paragraph; see also Morris, column 3, paragraph 2).

Response

10. To the extent that Applicants' arguments can be similarly applied to the new Kauffman et al. reference, the following comments are noted.

[1] Applicants argue, "As discussed in detail above, Kauffmann et al. fails to teach the claimed library of nucleic acid construct each of which comprises one or more copies of a cis element to which a transcription factor is already known to bind ... Kauffmann et al. teaches a method for identifying new cis elements from a diverse library of nucleic acid candidates" (e.g., see 7/28/04 Response, pages 8-9).

[2] Applicants argue, "If a library of of nucleic acid constructs each of which comprises one or more copies of a cis element to which a transcription factor is already known to bind Kauffmann's purpose of finding new cis elements would have been defeated. Thus, the cited references ... also fail to motivate one of ordinary skill in the art [to] modify the library in Kauffmann et al. in view of Morris et al. to arrive [at] the claimed invention" (e.g., see 7/28/04 Response, page 9).

This is not found persuasive for the following reasons:

[1] The Examiner contends that the arguments directed toward the Kauffman et al. reference above, have been adequately addressed in that section (which are incorporated in their entirety herein by reference).

[2] In response to applicant's argument that there is no suggestion to combine the references, the examiner recognizes that obviousness can only be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so found either in the references themselves or in the knowledge generally available to one of ordinary skill in the art. See *In re Fine*, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988)and *In re Jones*, 958 F.2d 347, 21 USPQ2d 1941 (Fed. Cir. 1992). In this case, one of ordinary skill in the art would have been motivated to use the variable

reporters as taught by Morris et al. because the variable reporters "provide a much more cost-effective approach to screening" i.e., parallel screening saves time and money (e.g., see Morris et al., column 11, lines 60-62). The use of "variable reporters" for money/time savings would not "defeat" Kauffman's purpose because it would not prevent the identification of the cis elements i.e., the "reporters" have nothing to do with whether or not the cis element is known or unknown.

Conclusion

Applicant's amendment necessitated any new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jon D Epperson whose telephone number is (571) 272-0808. The examiner can normally be reached Monday-Friday from 9:00 to 5:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Andrew Wang can be reached on (571) 272-0811. The fax phone number for the organization where this application or proceeding is assigned is (703) 872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (571) 272-1600.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Jon D. Epperson, Ph.D.
November 15, 2004